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Original Article

Pain after Palliative Radiotherapy for Spine Metastases

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Abstract

Aims: The purpose of the study was to evaluate the response to palliative radiotherapy in patients with painful spinal metastatic disease (SMD).
Materials and methods: Three hundred and fifty-five patients admitted to the Norwegian Radium Hospital for radiotherapy for painful SMD were included in a prospective study and were followed up 2 months later. The Brief Pain Inventory was used to assess pain. Analgesic consumption was recalculated into the daily oral morphine-equivalent dose. The radiotherapy-related response rates were calculated using the criteria of the International Bone Metastases Consensus Group (IBMCG), taking into account the use of concomitant analgesics. The response to radiotherapy was assessed as complete or partial and non-response as stable pain, pain progression or 'other'.
Results: Brief Pain Inventory forms were obtained at follow-up from 229 of the 355 patients. Two months after radiotherapy, the median self-reported worst pain decreased significantly, but the median oral morphine-equivalent dose increased from 40 to 60 mg ($P < 0.001$). Forty-three per cent of the patients reported pain relief, but a radiotherapy-related response was found in 37% of the patients. Overall correspondence between the patients' self-reported changes in pain experience and the IBMCG-based response categories was obtained in 63% of the patients.
Conclusions: The radiotherapy-related response rates in our study were lower than those reported previously in patients with bone metastases in general, which possibly indicates the presence of more complex pathophysiological mechanisms of pain in SMD.

Key words: Pain; radiotherapy; response criteria; response rates; spine metastases

Introduction

Spinal metastatic disease (SMD) is a feared complication of metastatic cancer and pain is the first clinical symptom in most patients. The aim of treatment is pain relief and the maintenance or restoration of function. Radiotherapy is the most common local treatment for SMD [1] and most studies present improvement in walking ability as the outcome of radiotherapy [2–6]. In most previous studies on radiotherapy-induced pain relief, patients with SMD were included together with patients with skeletal metastases at other localisations and were never evaluated separately [7–12], but some papers presented pain relief after radiotherapy in cohorts of patients with metastases in the spine [13,14].

The pathophysiological mechanisms of bone pain are complex and may include the release of chemical mediators, increased pressure within the bone, microfractures, stretching of the periosteum, together with pathological fractures and mechanical instability. In addition, a metastatic lesion in the spine may affect neurological structures, such as nerve roots, the cauda equina or the spinal cord, and cause neuropathic as well as nociceptive pain. Thus, patients with SMD probably differ from patients with bone metastasis at other localisations and the response rates to treatment of spinal metastases may therefore be lower in SMD patients than they are in patients with skeletal metastases of other localisations.

Any scientific assessment of pain and pain relief is complicated by the subjective nature of this measure, which is partly reflected in the wide range of published response rates to radiotherapy of painful bone metastases from 60 to 90% [15]. The reported response rate can be strongly influenced by considering the use of concomitant analgesics in the assessment of the response. Chow *et al.* [16] reported

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about a 70% response rate when response was evaluated by pain score alone, but when assessed by the integrated pain and analgesic score, the reported response rate was about 50%. However, most studies do not consider systematically the concomitant use of analgesics when the response rates to radiotherapy address pain relief [2,14,17], although consideration of the use of analgesics in the definition of response has a major effect on the reported outcome [15,18]. Maranzano *et al.* [14] investigated pain relief as the end point after radiotherapy for metastatic spinal cord compression and reported 57% of responders assessing the response as no pain after radiotherapy or pain requiring minor analgesics.

Other confounders that may influence the reported outcome are tumor-related therapy, such as chemotherapy and hormone therapy, together with steroids and co-analgesics. To provide consistency to the presentation of the results obtained in clinical trials, the International Bone Metastases Consensus Group (IBMCG) reached a consensus on how to combine the experience of pain and the use of analgesics when reporting the end points of palliative radiotherapy [19]. Harris *et al.* [7] reported an overall response calculated for evaluable patients according to the IBMCG and using worst pain scores as 66%.

The aim of the present study was to assess the patients' experience of pain 2 months after palliative radiotherapy, and to evaluate changes in the self-reported pain and the use of concomitant analgesics. Furthermore, we wanted to calculate the response rates to radiotherapy using the international defined response criteria and considering the use of concomitant analgesic as a confounding factor. In addition, we analysed possible prognostic factors for a radiotherapy-related response. Finally, we compared the patients' own experience of pain with the calculated radiotherapy-related response.

Materials and Methods

During the period from February 2007 to December 2008, all consecutive patients with painful spine metastases in the cervical, thoracic or lumbal spine who were admitted for radiotherapy at the Norwegian Radium Hospital were considered for this prospective study. The inclusion criteria were admittance for palliative radiotherapy for painful SMD, age above 18 years, ability to understand and speak the Norwegian language and consent to participate in the study. We excluded patients who were to receive radiotherapy after surgery or in-field re-irradiation and radiotherapy for paravertebral tumours without involving the spine or for intrathecal metastases.

The information obtained from the medical records included age, gender, primary cancer diagnosis, number of spinal metastases, number and localisation of non-spinal bone metastases and evidence of non-skeletal metastases. Registration of current systemic treatment included the use of high-dose corticosteroids, hormone therapy and chemotherapy.

Radiotherapy was applied as high-voltage irradiation with linear accelerators using daily fractions. Depending on the clinical situation, the patients received 8 Gy as a single fraction, 4 Gy × 5, 3 Gy × 10–12 or, exceptionally, 2 Gy × 25. The target volume comprised the vertebral bodies, the processus tranversi and any soft tissue component of the lesion, as imaged by computed tomography or magnetic resonance imaging. The adjoining proximal and distal vertebrae were included in the target field.

The patients were interviewed by a trained research nurse immediately before or as soon as possible after the start of radiotherapy. All patients who received a single fraction were interviewed on the same day as the radiotherapy was carried out. Patients who received multiple fractions were interviewed before the radiotherapy was completed and less than 2 weeks after the onset of the radiotherapy.

Using a predefined questionnaire, the patients were asked about symptoms related to SMD, such as local back pain, irradiating pain, sensory deficit, motor deficit in the upper or lower extremities and bladder or rectum dysfunction. The patients were also asked about their place of living (at home versus nursing centre) and the use of home-nursing services. The ambulatory status of the patients before the onset of treatment was recorded using question 7 (mobility) of the Barthel ADL functional score [20,21] (0 points, immobile; 1 point, wheelchair; 2 points, walks with help; 3 points, independent; patients who scored 0–1 were defined as non-ambulatory and those who scored 2–3 were defined as ambulatory). The performance status was assessed using the Karnofsky performance score [22].

The validated Norwegian version of the Brief Pain Inventory (BPI) was used for the evaluation of pain intensity [23,24], by assessing the worst pain, average pain and least pain experienced during the previous 24 h as well as 'pain right now'. A numeric rating scale was used where 0 was 'no pain' and 10 was 'pain as bad as you can imagine'. Worst pain was used as the principal outcome measure of radiotherapy response. Opioid consumption during the previous 24 h was registered by assessing the drug name, the daily dose and the route of administration. All opioids were converted into the oral morphine-equivalent dose (OMED).

Two months after the onset of the radiotherapy, the research nurse contacted the patients via telephone and completed the BPI during the interview. The localisation of the pain was recorded, and the patients were asked to address the pain intensity related to the treated site of the spine. Place of living, use of home nursing and the Karnofsky performance score were also recorded at the 2 month follow-up. The ambulatory status was recorded using question 7 of the Barthel ADL functional score. A change in worst pain from baseline to follow-up was assessed as unchanged pain if the 2 month follow-up score of self-reported pain was 1 point below, equal or 1 point above the baseline value. A change of 2 or more points above or below the baseline value was categorised as increased pain or pain relief, respectively.

The assessment of radiotherapy response taking into consideration the potential confounding effect of pain medication was carried out according to the IBMCG [7,19,25], based on the BPI records of worst pain and OMED. The